A new approach to arylaliphatic 1,5-, 1,6-, and 1,7-dicarbonyl compounds and their monoacetals based on direct anodic oxidation of 1-phenyl- and benzo[*c*]cycloalkenes

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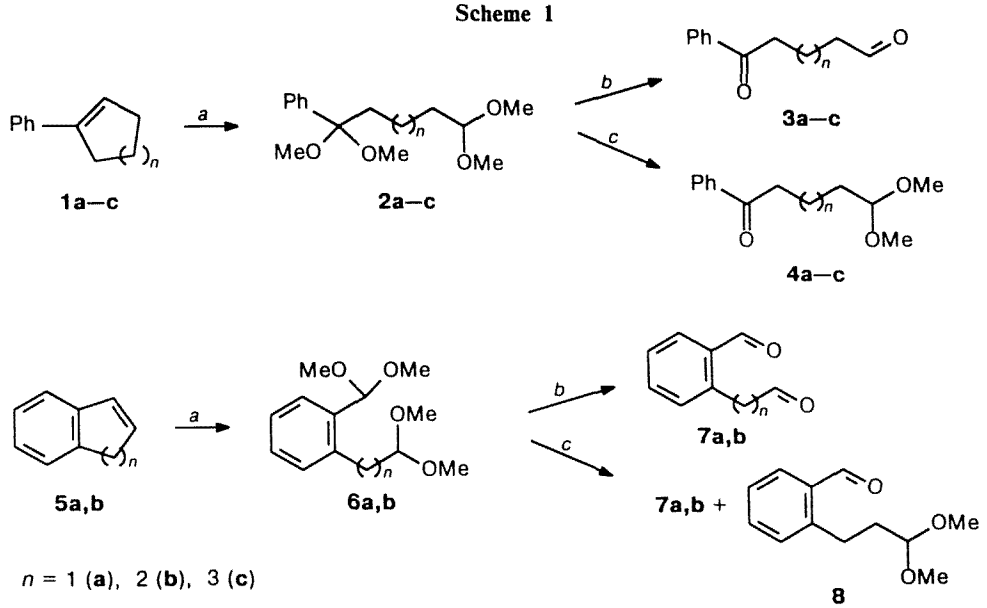
A new simple approach to ω-benzoylalkanals, 2-(ω-formylalkyl)benzaldehydes, and their monoacetals was developed based on direct anodic oxidation of 1-phenylcycloalkenes and benzo[*c*]cycloalkenes in methanol followed by acid hydrolysis of the electrolysis products. The target products are obtained in 53—72 % yields.

Key words: 4-, 5-, and 6-benzoylalkanals, 4-, 5-, and 6-benzoyl-1,1-dimethoxyalkanes, homophthalaldehyde, 2-(2-formylethyl)- and 2-(2,2-dimethoxyethyl)benzaldehydes, anodic oxidation, 1-phenylcycloalkenes, benzo[*c*]cycloalkenes.

Dicarbonyl compounds with 1,5- and more remote carbonyl groups are key intermediates in the synthesis of carbocyclic and heterocyclic compounds containing 5 to 7 carbon atoms in the ring.[1—5] These compounds are usually prepared by ozonolysis or an equivalent cleavage of cycloalkenes[6] and their epoxides.[7] 5-Oxoalkanals are also obtained by the condensation of enamines with α,β-unsaturated aldehydes;[8] 1,5-dialdehydes are formed on acid hydrolysis of the products of cycloaddition of α,β-unsaturated aldehydes to vinyl ethers.[9] Arylaliphatic 1,5-, 1,6-, and 1,7-dicarbonyl compounds have also been obtained by the ozonolysis of indene,[3,10,11] benzo[*c*]cyclohexene (1,2-dihydronaphthalene),[12] and 1-phenylcyclopentene,[13] by oxidative cleavage of α-phenylepoxycycloalkanes under the action of pyridinium chlorochromate,[7] and by condensation of acrolein with enamine derived from acetophenone.[4]

In this paper we report a new approach to arylaliphatic dicarbonyl compounds containing 1,5- and more remote carbonyl groups. The approach involves direct anodic oxidation of 5—7-membered conjugated phenylcycloalkenes **1** or the corresponding benzocycloalkenes **5** in methanol (Scheme 1). Subsequent hydrolysis of the electrolysis products **2** and **6** with dilute sulfuric acid

Scheme 1



Reagents and conditions: *a*. 6 F mol^{-1}, MeOH, Bu_4NBF_4, 60 °C; *b*. 10 % H_2SO_4, 50 °C, 2 h; *c*. 10 % H_2SO_4, 20 °C, 20 min.

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leads to dicarbonyl compounds **3** and **7** or their monoacetals **4** and **8**.

The development of this method for the synthesis of these valuable multipurpose compounds was also stimulated by our desire to extend the known methodology for the electrochemical cleavage of the olefinic bonds in styrenes[14—16] to aryl- and benzo-substituted cycloalkenes. The successful solution of this problem, considered in detail in our previous paper,[17] allowed us to carry out the electrochemical transformation of compounds **1** and **5** into acetal-ketal derivatives of dicarbonyl compounds **2** and **6**. The process occurs most efficiently under the conditions of direct anodic oxidation of **1** and **5** at 60 °C in methanol in an undivided cell with a graphite anode and a stainless-steel cathode, using Bu_4NBF_4 as a supporting electrolyte, and when 6 F of electricity per mole of the starting substrate is passed. Subsequent acid hydrolysis of intermediates **2** and **6** with 10 % aqueous H_2SO_4 affords different products depending on the reaction conditions. For example, upon moderate heating (50 °C, 2 h), compounds **2** and **6** are completely converted into ω-benzoylalkanals **3** and 2-(ω-formylalkyl)benzaldehydes **7**. At ~20 °C for 20 min; only the ketal groups in intermediates **2a—c** and mostly the benzyl acetal group in compound **6b** are hydrolyzed to give monoacetals **4a—c** and **8**. The hydrolysis of **6a** gives 2-(formylmethyl)benzaldehyde (**7a**) in both cases (Table 1).

Table 1. Anodic oxidation of 1-phenylcycloalkenes **1a—c** and benzo[*c*]cycloalkenes **5a,b** and hydrolysis of the compounds obtained[a]

Cycloalkene	Electrolysis product[b]	Yield (%)[c] of the electrolysis product	Hydrolysis conditions[d]	Hydrolysis product	Yield (%)[e]
1a	**2a**	62	*A*	**3a**	90 (56)
			B	**4a**	93 (57)
1b	**2b**	58	*A*	**3b**	92 (53)
			B	**4b**	94 (54)
1c	**2c**	76	*A*	**3c**	95 (72)
			B	**4c**	96 (72)
5a	**6a**	75	*A*	**7a**	87 (65)
			B	**7a**	85 (64)
5b	**6b**	61	*A*	**7b**	87 (53)
			B	**8**[f]	65 (40)

[a] Using a graphite anode, a stainless-steel cathode, an 0.1 *M* methanolic solution Bu_4NBF_4 as the supporting electrolyte, 6 F mol^{-1}, current density 100 mA cm^{-2}, and 60 °C. [b] Along with compounds **2** and **6**, intermediate 1,2-dimethoxy-1-phenylcycloalkanes and 1,2-dimethoxybenzo[*c*]cycloalkanes were isolated in 3—17 % yields.[17] [c] Isolated product. [d] *A*: 10 % H_2SO_4, 50 °C, 2 h. *B*: 10 % H_2SO_4, 20 °C, 20 min. [e] Yields of the isolated products based on compounds **2** and **6** (the yield based on **1** and **5** are given in parentheses). [f] Compound **7b** is also formed in 25 % yield based on **6**.

The structures of obtained compounds **3a—c**, **7a,b**, **4a—c**, and **8** were confirmed by ^1H and ^{13}C NMR spectroscopy data.

Thus, we developed a new facile method for the synthesis of arylaliphatic 1,5-, 1,6-, and 1,7-dicarbonyl compounds, *viz.*, ω-benzoylalkanals **3**, 2-(ω-formylalkyl)benzaldehydes **7**, and their monoacetals **4** and **8**, from available phenylcycloalkenes and benzocycloalkenes.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker WM-250 and Bruker AM-300 spectrometers in $CDCl_3$ using tetramethylsilane as the internal standard. Mass spectra were obtained on a Varian MAT-311A instrument (EI, 70 eV). GLC analysis was carried out on a Varian 3700 chromatograph (flame ionization detector, 2000×3 mm glass columns, and 5 % Carbowax 20M on Inerton AW 100/120 and 5 % XE-60 on Chromaton N-AW 100/120 as stationary phases). Column chromatography was carried out using L 40/100 μm silica gel. Commercial 1-phenylcyclohexene **1b** and indene **5a** of the "pure" grade were used; they were additionally purified by distillation. Compounds **1a,c**, **5a**, and Bu_4NBF_4 were obtained by known procedures.[17] Methanol was dried by distillation over magnesium methoxide.

Anodic oxidation of 1-phenylcycloalkenes 1a—c and benzo[*c*]cycloalkenes 5a,b. Synthesis of acetal-ketals 2 and bis-acetals 6 (general procedure). Electrooxidation of **1a—c** and **5a,b** (15 mmol) was carried out under galvanostatic conditions in an undivided cell described previously.[15] The conditions of the experiments are listed in Table 1. MeOH was distilled from the electrolyzate obtained, the residue was extracted with hexane (2×30 mL), and the extract was concentrated. Fractional vacuum distillation or chromatography (using a 50 : 1 light petroleum—ethyl acetate mixture as the eluent) of the residue gave the corresponding product **2** or **6** (the yields are listed in Table 1, and the analytical data were reported previously[17]).

Preparation of ω-benzoylalkanals 3 and 2-(ω-formylalkyl)benzaldehydes 7 (general procedure). A mixture of 10 % aqueous H_2SO_4 (50 mL) and compound **2** or **6** (10 mmol) was stirred at 50 °C until the intermediate monoacetal was completely converted (2 h, GLC monitoring). The reaction mixture was extracted with ether (4×20 mL), and the ethereal extracts were washed with water and a saturated solution of $NaHCO_3$ and concentrated. The products were chromatographed (using a 95 : 5 light petroleum—ethyl acetate mixture as the eluent) to give ω-benzoylalkanals **3** and 2-(ω-formylalkyl)benzaldehydes **7**, whose yields are listed in Table 1. The physicochemical parameters and ^1H NMR spectra correspond to those of the same compounds prepared by alternative methods.[4,7,10]

4-Benzoylbutanal (3a)[4]. ^{13}C NMR ($CDCl_3$), δ: 16.52, 37.28, and 43.06 (t); 127.97, 128.63, and 133.15 (d); 136.72 (s); 199.29 (s); 201.95 (d, CHO). MS, *m/z* (I_{rel}(%)): 176 (2) $[M]^+$, 148 (11), 121 (12), 120 (15), 105 (100), 77 (62).

5-Benzoylpentanal (3b)[7,18]. ^{13}C NMR ($CDCl_3$), δ: 21.50, 23.40, 37.94 and 43.51 (t); 127.84, 128.44, and 132.90 (d); 136.67 (s); 199.66 (s); 202.32 (d, CHO). MS, *m/z* (I_{rel}(%)): 190 (5) $[M]^+$, 162 (9), 146 (16), 133 (22), 120 (57), 105 (100).

6-Benzoylhexanal (3c).[7] ^{13}C NMR ($CDCl_3$), δ: 21.87, 23.87, 28.75, 38.16, and 43.66 (t); 127.98, 128.56, and 132.94 (d); 136.95 (s); 199.96 (s); 202.39 (d, CHO). MS, *m/z* (I_{rel}(%)):

204 (5) $[M]^+$, 202 (4), 186 (7), 161 (8), 147 (12), 133 (10), 121 (13), 120 (52), 105 (100).

2-(Formylmethyl)benzaldehyde (homophthalaldehyde) (7a).[10] MS, *m/z* (I_{rel}(%)): 148 (5) $[M]^+$, 147 (8), 134 (25), 131 (20), 120 (92), 119 (100).

2-(2-Formylethyl)benzaldehyde (7b).[12] ^{1}H NMR ($CDCl_3$), δ: 3.26 (t, 2 H); 3.69 (t, 2 H); 7.20—7.75 (m, 4 H), 9.72 (t, 1 H), 10.06 (s, 1 H). ^{13}C NMR ($CDCl_3$), δ: 25.41 and 44.80 (t); 127.50, 130.92, 133.72, and 134.10 (d); 133.59 and 142.66 (s); 192.83 and 201.04 (d). MS, *m/z* (I_{rel}(%)): 162 (12) $[M]^+$, 161 (22), 160 (43), 159 (18), 150 (22), 149 (100), 133 (56), 132 (24), 131 (50), 119 (55).

Preparation of monoacetals 4 and 8 (general procedure). A mixture of 10 % aqueous H_2SO_4 (10 mL) and acetal **2** or **6** was stirred at ~20 °C until it was completely converted (20 min, GLC monitoring). The reaction mixture was treated as described above for compounds **3** and **7** to give monoacetals **4** from **2**, dialdehyde **7a** from **6a**, and monoacetal **8** from **6b**, whose yields are listed in Table 1.

4-Benzoylbutanal dimethylacetal (4a). ^{1}H NMR ($CDCl_3$), δ: 1.67 (m, 2 H); 1.79 (m, 2 H); 2.98 (t, 2 H); 3.32 (s, 6 H); 4.37 (t, 1 H); 7.42—7.59 (m, 3 H), 7.95 (m, 2 H).

5-Benzoylpentanal dimethylacetal (4b). ^{1}H NMR ($CDCl_3$), δ: 1.44 (m, 2 H); 1.63 (m, 2 H); 1.77 (m, 2 H); 2.98 (t, 2 H); 3.30 (s, 6 H); 4.37 (t, 1 H); 7.40—7.58 (m, 3 H); 7.94 (m, 2 H).

6-Benzoylhexanal dimethylacetal (4c). ^{1}H NMR ($CDCl_3$), δ: 1.39 (m, 4 H); 1.61 (m, 2 H); 1.76 (m, 2 H); 2.97 (t, 2 H); 3.31 (s, 6 H); 4.36 (t, 1 H); 7.41—7.59 (m, 3 H); 7.95 (m, 2 H).

2-(2,2-Dimethoxyethyl)benzaldehyde (8). ^{1}H NMR ($CDCl_3$), δ: 1.89 (m, 2 H); 3.08 (t, 2 H); 3.32 (s, 6 H); 4.38 (t, 1 H); 7.25—7.60 (m, 3 H); 7.79 (m, 1 H), 10.23 (s, 1 H).

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